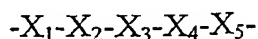


CLAIMS

1. A polypeptide comprising
(i) a leader sequence, the leader sequence comprising
5 (a) a secretion pre sequence, and
(b) the following motif:



10 where X_1 is phenylalanine, tryptophan, or tyrosine, X_2 is
isoleucine, leucine, valine, alanine or methionine, X_3 is
leucine, valine, alanine or methionine, X_4 is serine or
threonine and X_5 is isoleucine, valine, alanine or methionine;
and

- 15 (ii) a desired protein heterologous to the leader sequence.

2. A polypeptide according to Claim 1 wherein X_1 is phenylalanine.

3. A polypeptide according to Claim 1 or 2 wherein X_2 is isoleucine.

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4. A polypeptide according to any one of the preceding claims wherein
 X_3 is valine.

5. A polypeptide according to any one of the preceding claims wherein
25 the amino acids of the motif are included in the polypeptide as substitutes,
for naturally occurring amino acids.

6. A polypeptide according to any one of the preceding claims wherein
 X_5 is isoleucine.

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7. A polypeptide according to any one of the preceding claims wherein the motif is -Phe-Ile-Val-Ser-Ile-.
8. A polypeptide according to any one of the preceding claims wherein the secretion pre sequence is an albumin secretion pre sequence or a variant thereof.
9. A polypeptide according to Claim 8 wherein X_1 , X_2 , X_3 , X_4 and X_5 are at positions -20, -19, -18, -17 and -16, respectively, in place of the naturally occurring amino acids at those positions, wherein the numbering is such that the -1 residue is the C-terminal amino acid of the native albumin secretion pro sequence and where X_1 , X_2 , X_3 , X_4 and X_5 are amino acids as defined in any one of Claims 1 to 7.
10. A polypeptide according to Claim 8 or 9 wherein the albumin secretion pre sequence or variant thereof is a human albumin secretion pre sequence or a variant thereof.
11. A polypeptide according to Claim 10 comprising the secretion pre sequence MKWVFIVSILFLFSSAYS.
12. A polypeptide according to any one of the preceding claims wherein the leader sequence comprises a secretion pro sequence.
13. A polypeptide according to Claim 12 wherein the albumin secretion pre sequence or variant thereof is fused by a peptide bond at its C-terminal end to the N-terminal amino acid of a secretion pro sequence, or variant thereof, thereby to form a pre-pro sequence.

14. A polypeptide according to Claim 12 or 13 wherein the secretion pro sequence is an albumin secretion pro sequence or variant thereof.

15. A polypeptide according to Claim 14 wherein the albumin secretion pro sequence is human serum albumin secretion pro sequence or variant thereof.

16. A polypeptide according to Claim 14 or 15 wherein the secretion pro sequence motif is the yeast MF α -1 secretion pro sequence or variant thereof.

17. A polypeptide according to Claim 12 comprising the sequence:

MKWVFIVSILFLFSSAYSRY¹Y²Y³Y⁴Y⁵

wherein Y¹ is Gly or Ser, Y² is Val or Leu, Y³ is Phe or Asp, Y⁴ is Arg or Lys and Y⁵ is Arg or Lys, or variants thereof.

18. A polypeptide according to Claim 17 wherein Y¹ is Gly, Y² is Val and Y³ is Phe; or Y¹ is Ser, Y² is Leu and Y³ is Asp.

19. A polypeptide according to Claim 17 or 18 wherein Y⁴ is Arg and Y⁵ is Arg; Y⁴ is Lys and Y⁵ is Arg; Y⁴ is Lys and Y is Lys; or Y⁴ is Arg and Y⁵ is Lys.

20. A polypeptide according to any one of claims 1 to 7 wherein at least part of said motif is present in the secretion pre-sequence.

21. A polypeptide according to any one of the preceding claims wherein the sequence of the desired protein is fused at its N-terminal end to the C-terminal amino acid of the leader sequence.
- 5 22. A polypeptide according to any one of the preceding claims where the desired protein is albumin or a variant, fragment or fusion thereof.
- 23 A polypeptide according to Claim 22 wherein the albumin is human albumin.
- 10 24. A polypeptide according to any one of Claims 1 to 21 wherein the mature polypeptide is transferrin or a variant, fragment or fusion thereof.
25. A polypeptide according to Claim 24 wherein the transferrin is human transferrin.
- 15 26. An isolated polynucleotide comprising a sequence that encodes the motif defined by any preceding claim.
- 20 27. A polynucleotide according to Claim 26 comprising the sequence of SEQ ID No. 15.
28. A polynucleotide according to Claim 26 comprising the sequence of SEQ ID No. 16.
- 25 29. A polynucleotide according to Claim 26 comprising the sequence of SEQ ID No. 17.
- 30 30. A polynucleotide according to Claim 26 comprising the sequence of SEQ ID No. 18.

31. A polynucleotide according to Claim 26 comprising the sequence of SEQ ID No. 34.
- 5 32. A polynucleotide according to Claim 30 or 31 comprising the sequence of SEQ ID No. 24.
33. A polynucleotide according to Claim 32 comprising the sequence of SEQ ID No. 25 or a variant thereof, which variant has the leader sequence
10 of SEQ ID No.24 and encodes a variant or fragment of the albumin encoded by SEQ ID No.25.
34. A polynucleotide according to Claim 30 or 31 comprising the sequence of SEQ ID No. 27.
- 15 35. A polynucleotide according to Claim 34 comprising the sequence of SEQ ID No. 21 or a variant thereof, which variant has the leader sequence of SEQ ID No.27 and encodes a variant or fragment of the albumin encoded by SEQ ID No.21.
- 20 36. A polynucleotide comprising the sequence of SEQ ID No. 21 or fragment thereof.
37. A polynucleotide according to any one of Claims 33, 35 or 36
25 wherein the polynucleotide comprises a DNA sequence being a contiguous or non-contiguous fusion of a DNA sequence encoding a heterologous protein with either the DNA sequence SEQ ID No. 25 or the DNA sequence SEQ ID No. 21.

38. A polynucleotide which is the complementary strand of a polynucleotide according to any one of claims 26 to 37.

39. A polynucleotide according to any one of Claims 26 to 38
5 comprising an operably linked transcription regulatory region.

40. A polynucleotide according to Claim 39 wherein the transcription regulatory region comprises a transcription promoter.

10 41. A self-replicable polynucleotide sequence comprising a polynucleotide according any one of Claims 26 to 40.

42. A cell comprising a polynucleotide according to any one of Claims 26 to 41.

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43. A cell according to Claim 42 which is a eukaryotic cell.

44. A cell according to Claim 43 which is a fungal cell.

20 45. A cell according to Claim 44 which is an *Aspergillus* cell

46. A cell according to Claim 44 which is a yeast cell.

47. A cell according to Claim 46 which is a *Saccharomyces*,
25 *Kluyveromyces*, *Schizosaccharomyces* or *Pichia* cell.

48. A cell culture comprising a cell according to any one of Claims 42 to 47 and culture medium.

49. A cell culture according to Claim 48 wherein the medium contains a mature desired protein as a result of the production of a polypeptide as defined in any one of Claims 1 to 22.

5 50. A process for producing a mature desired protein, comprising (1) culturing a cell according to any one of Claims 42 to 47 in a culture medium wherein the cell, as a result of the production of a polypeptide as defined in any one of Claims 1 to 25, secretes a mature desired protein into the culture medium, and (2) separating the culture medium, containing the secreted
10 mature protein, from the cell.

51. A process according to Claim 50 additionally comprising the step of separating the mature desired protein from the medium and optionally further purifying the mature desired protein.

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52. A process according to Claim 51 additionally comprising the step of formulating the thus separated and/or purified mature desired protein with a therapeutically acceptable carrier or diluent thereby to produce a therapeutic product suitable for administration to a human or an animal.

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